UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/807,603	04/16/2001	Satoru Todo	067242/0148	2083

22428 7590 11/03/2004

FOLEY AND LARDNER
SUITE 500
3000 K STREET NW
WASHINGTON, DC 20007

EXAMINER	
KWON, BRIAN YONG S	

ART UNIT	PAPER NUMBER
1614	

DATE MAILED: 11/03/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/807,603	TODO, SATORU	
	Examiner	Art Unit	
	Brian S Kwon	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 May 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *48,101,104,106,107,109 and 111-113* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *48,101,104,106,107,109 and 111-113* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Application

1. Receipt is acknowledged of applicant's filing of the instant application as a Request for Continued Examination (RCE) under 37 CFR 1.114.

2. Acknowledgement is made of applicant's filing of an amendment on May 24, 2004. By the amendment, claims 48, 101, 104, 106-107, 109 and 111 have been amended and claims 112 and 113 have been newly added.

Claim Rejections - 35 USC §103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

3. Claims 48, 101, 104, 106-107, 109 and 111-113 are rejected under 35 U.S.C. 103(a) as obvious over Sonnino et al. (Digestive Diseases and Sciences, Vol. 42, No.5, May 1997) in view of Khau et al. (US 5986106).

Sonnino discloses PX-13 as a sPLA2 inhibitor, and it further states that PLA2 released during ischemia is a type-II substance, that sPLA2 contributes to ischemic reflow, and that control of sPLA2 activity protects tissue fragments from ischemia and reflow in cold preservation graft study (abstract and page 973, column 1, para. 2). More specifically, Sonnino teaches or suggests the use of sPLA2 inhibitors for ischemic-reperfusion injury (page 980, column 1, lines 1-13).

Khau teaches the use of the claimed compounds represented by the formula (I), namely [[3-(2-amino-1,2-dioxoethyl)-2-ethyl-1-(phenylmethyl)-1H-indole-4-yl]oxy]acetic acid and its sodium salt, as sPLA2 inhibitor (column 12, line 52; Example 1) .

The teaching of Sonnino differs from the claimed invention in the use of the specific sPLA2 inhibitor represented by the formula (I) for the treatment of ischemia reperfusion injury. To incorporate such teaching into the teaching of the Sonnino, would have been obvious in view of Khau teaches the use of [[3-(2-amino-1,2-dioxoethyl)-2-ethyl-1-(phenylmethyl)-1H-indole-4-yl]oxy]acetic acid and its sodium salt as sPLA2 inhibitor.

One having ordinary skill in the art would have known that sPLA2 contributes to ischemia-reperfusion injury and inhibition of sPLA2 would be useful in treating ischemia-reperfusion injury. One having ordinary skill in the art would have expected that any compounds that inhibit the secretion of sPLA2 would have similar therapeutic utility in the treatment of ischemia-reperfusion injury. Furthermore, one having ordinary skill in the art would have been motivated to administer well known sPLA2 (as taught by Khau), with the reasonable expectation of success, to treat ischemia-reperfusion injury. One having ordinary skill in the art would have motivated to make such modification to extend the usage of the claimed sPLA2 inhibitor, namely

[[3-(2-amino-1,2-dioxoethyl)-2-ethyl-1-(phenylmethyl)-1H-indole-4-yl]oxy]acetic acid, in the treatment of ischemia-reperfusion injury.

Response to Arguments

4. Applicant's arguments filed May 24, 2003 have been fully considered but they are not persuasive.

Applicant's argument takes position that one having ordinary skill in the art would not expect effective treatment of ischemia-reperfusion injury occurring in organs, such as heart, liver, kidney and pancreas since a variety factors are involved in ischemia-reperfusion injury in different organs in different ratios.

Applicant's argument is not persuasive at all. Contrary to the applicant's argument, it was known at the time of the invention was made that the effective agent for the treatment of ischemia-reperfusion injury occurred in the intestinal tract would work for treating the ischemia reperfusion injury in other organs including liver, kidney, pancreas and heart. See Moldawer et al. (US 6086868). Moldawer teaches the use of an effective amount of interleukin-10 for the treatment or prevention of ischemia reperfusion injury in a patient having an ischemic condition caused by surgery or injury to an organ after reperfusion, wherein ischemia reperfusion injury occurs in heart, liver, pancreas, kidney and intestines (column 1, lines 9-28; column 1, line 52 thru column 2, line 11; claims). Thus, one having ordinary skill in the art would expect similar therapeutic effects in the treatment of ischemia-reperfusion injury occurring in heart, liver, pancreas and kidney.

Applicant's argument takes position that the effective treatment of organs containing a small amount of type II sPLA2 cannot be rendered obvious by the result of treatment of ischemia reperfusion injury in intestine which contains high amounts of type II PLA2.

This is spurious argument. Throughout the specification, applicant describes the claimed compounds as type II PLA2 inhibitor. Similar to the Sonnino's teaching, applicant makes a correlation between the activity of type II PLA2 inhibitor and the pathophysiology of ischemia reperfusion in intestine, and further probes about the utility of said type II PLA2 inhibitor in the treatment of ischemia-reperfusion in other organs such as heart, kidney, liver and pancreas. In other words, the instant invention relates to the role of type II PLA2 in pathophysiology of ischemia-reperfusion injury and the utility of the claimed compounds having type II PLA2 inhibitor in the treatment of ischemia-reperfusion injury in multiple organs including kidney, liver, intestine, heart and pancreas. Therefore, in light of the instant specification, the reader would understand that type II PLA2 inhibiting activity of the claimed compounds is critical to the claimed invention and would provide a therapeutic utility in ischemia reperfusion injury associated with the increase of type II PLA2 activity, which this notion is consistent with the state of the prior art at the time of the invention was made (as shown by Sonnino).

Contrary to the what is generally taught in the prior art and the what is generally disclosed in the instant specification mentioned above, applicant alleges that the claimed type II PLA2 inhibitors are effective in treating ischemia reperfusion injury in heart, liver, pancreas and kidney where no type II PLA2 is presented. In other words, it appears from reading applicant's remarks that type II PLA2 is not a contributing factor for ischemia-reperfusion injury in liver, kidney, heart and pancreas. As discussed above, there is absolutely no basis for this claim found

in the instant specification. Therefore, based on the instant specification and the state of the art consistent with the instant invention, the examiner cannot consider the submitted documents (Attachments B-C) as overcoming evidences to the rejection under 35 USC 103(a).

Conclusion

5. No Claim is allowed.

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Kwon whose telephone number is (571) 272-0581. The examiner can normally be reached Tuesday through Friday from 9:00 am to 7:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low, can be reached on (571) 272-0951. The fax number for this Group is (703) 872-9306.

Any inquiry of a general nature of relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Brian Kwon
Patent Examiner
AU 1614

VICKIE KIM
PRIMARY EXAMINER